REMARKS/ARGUMENTS

Claims 1-35 were pending in the subject application. Of these, claims 5, 6, 9, 13, 14, 21, 22, 24, and 25 have been withdrawn from consideration. Claims 1, 3, 7, 10, 11, 12, 15, 23, 26, 33, have been amended to redefine the scope of the invention. Claims 2, 4, 5, 8, 9, 13, 14, 21, 22, 24, 25, and 36-37 have been cancelled. Thus claims 1, 3, 7, 10-12, 15-20, 23, and 26-35 are currently under consideration. Support for the claim amendments can be found in the specification as filed, at for example paragraphs 0026-0031 in the specification as filed. Applicants have made these amendments without relinquishing their right to pursue patent protection for unclaimed subject matter in a subsequent application.

I. Rejections Under 35 USC 112, second paragraph:

In the Office Action mailed December 28, 2007 the Examiner rejected Claims 1-4, 7-8, 10-12, 15-20, 23, and 26-37 under U.S.C. 112, second paragraph.. The Examiner stated that because "Ret receptor kinase" and other receptors disclosed in the instant application are identified by name, and not by structure, that the metes and bounds of the terms used are allegedly not clear.

In response, applicants respectfully disagree. However, in order to expedite prosecution, applicants have amended the instant claims to redefine the scope of the invention. Applicants have modified the claims to encompass only a hybrid receptor comprising a modified extracellular domain of human Ret protein wherein amino acid substitutions occur only at residues selected from Cys 609, Cys611, Cys618, Cys620, Cys630 or Cys634, and result in one or more unpaired cysteine residues being available for Ret dimer formation. The elected modification C634W, as in claim 7, is one such modification.

Applicants respectfully contend that the meaning of "human Ret kinase" in the claims is clear. There is only one gene coding for human Ret kinase (see NCBI Gene database, GeneID: 5979; http://www.ncbi.nlm.nih.gov/) and this kinase is unambiguously identified in the instant application by description, multiple references, and the experimental details for preparing a chimeric receptor. As

described in applicants previous response, one of skill in the art would recognize and understand what is meant by "Ret kinase." The term "Ret" is not an arbitrary designation for this gene, but is the approved gene symbol of the Human Gene Nomenclature Committee (see http://www.genenames.org/; part of HUGO). It is a widely used and accepted name for this gene, as evidenced by the exhibits previously submitted to the Examiner (e.g. from NCBI Gene Database; deVita, a standard oncology text; and Wikepedia). Thus it is not necessary to define what is meant by the term "human Ret kinase" in structural terms as there is no ambiguity likely to be created by the use of this term in the instant claims. Ret is the standard nomenclature for this gene.

The Examiner indicated that names of receptors change over time, or are named differently by different inventors or scientists. This may be true in certain cases, and Ret has been known in the past by other names, but as of the time of filing the instant application Ret was the standard and accepted name of this gene. More importantly, applicants are not aware of any other gene which has been given the name Ret, either officially or unofficially. If other genes had also been given the name Ret, this could potentially lead to ambiguity in the meaning of a term, but occasional use of an alternative name for Ret should not.

Applicants recognize that there may be polymorphisms or variants of human Ret kinase, as for most human genes. However, this again will not lead to ambiguity in the instant claims, and one of skill in the art will recognize the term "human Ret kinase" to mean any of such products of the human Ret gene. Applicants invention as described in the instant claims is not dependent on any given polymorphism or variant of human Ret. Rather, it is the particular Cys amino acid substitutions in the Ret extracellular domain that are critical to the instant invention. The invention will work with any human Ret extracellular domain sequence that includes the Cys substitutions as described in the instant claims.

Accordingly, in view of the above arguments and amendments, applicants respectfully submit that all rejections under 35 USC 112 have been overcome and request their withdrawal.

II. Rejections Under 35 USC 102

In the Office Action mailed December 28, 2007 the Examiner rejected Claims 1-4, 7-8, 10-12, 15-20, 23, and 26-37 under U.S.C. 102(b), as being anticipated by Rizzo et al. (1996) J. Biol. Chem. 271(46):29497-29501. The Examiner stated that Rizzo et al. discloses a hybrid receptor which is an EGFR/RET chimera (on pages 29498-29499), and that the "claim limitations do not exclude the receptors of Rizzo et al. because the claims recite receptors by name only."

In response, applicants respectfully point out that the chimeric receptors disclosed in Rizzo et al. are composed of an extracellular domain of EGFR fused to a catalytic kinase domain of Ret, wherein either a wild type Ret kinase domain or a mutant Ret kinase domain (i.e.MEN2B Ret) with a single point mutation that confers constitutive activity is used. In either case, the ligand EGF was used to activate the activity of the Ret kinase domain, and the effects of Ret kinase on cells could thus be investigated. In contrast, applicants hybrid receptor as described in the amended claims of the instant invention comprises a human Ret extracellular domain fused to the kinase domain of a heterologous receptor kinase, wherein the Ret extracellular domain comprises a modification that confers constitutive, ligand-independent activity on the hybrid receptor kinase. In the instant invention, in contrast to Rizzo et al., the Ret extracellular domain of the hybrid receptor confers ligand independent activity, and for example allows one to investigate the cellular effects of the heterologous kinase domain. In Rizzo et al. EGFR is used as the extracellular domain in order to confer EGF-activation on the Ret kinase domain of the hybrid receptor. Rizzo et al. do not disclose any hybrid receptor that uses a human Ret extracellular domain comprising a modification that confers constitutive, ligand-independent activity on the hybrid receptor kinase, and thus cannot anticipate the instant invention.

Accordingly, in view of the above arguments, applicants respectfully submit that all rejections under 35 USC 102 have been overcome and request their withdrawal.

III. Conclusion

In view of the arguments and amendments set forth above, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection, and that a timely Notice of Allowance be issued in this case.

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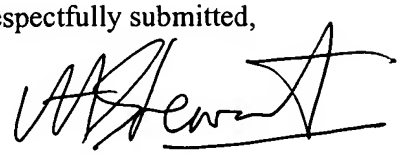
Respectfully submitted,



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